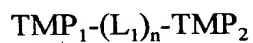
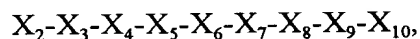


The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. A compound that binds to an mpl receptor comprising the structure



wherein  $\text{TMP}_1$  and  $\text{TMP}_2$  are each independently selected from the group of core compounds comprising the structure:



wherein,

15  $\text{X}_2$  is selected from the group consisting of Glu, Asp, Lys, and Val;

$\text{X}_3$  is selected from the group consisting of Gly and Ala;

$\text{X}_4$  is Pro;

$\text{X}_5$  is selected from the group consisting of Thr and Ser;

$\text{X}_6$  is selected from the group consisting of Leu, Ile, Val, Ala, and Phe;

20  $\text{X}_7$  is selected from the group consisting of Arg and Lys;

$\text{X}_8$  is selected from the group consisting of Gln, Asn, and Glu;

$\text{X}_9$  is selected from the group consisting of Trp, Tyr, and Phe;

$\text{X}_{10}$  is selected from the group consisting of Leu, Ile, Val, Ala, Phe, Met, and

Lys;

25  $\text{L}_1$  is a linker; and

$n$  is 0 or 1;

and physiologically acceptable salts thereof.

- 30 2. The compound according to Claim 1 wherein said  $\text{TMP}_1$  and  $\text{TMP}_2$  are independently selected from the group consisting of:

$X_2-X_3-X_4-X_5-X_6-X_7-X_8-X_9-X_{10}-X_{11}$ ;  
 $X_2-X_3-X_4-X_5-X_6-X_7-X_8-X_9-X_{10}-X_{11}-X_{12}$ ;  
 $X_2-X_3-X_4-X_5-X_6-X_7-X_8-X_9-X_{10}-X_{11}-X_{12}-X_{13}$ ;  
 $X_2-X_3-X_4-X_5-X_6-X_7-X_8-X_9-X_{10}-X_{11}-X_{12}-X_{13}-X_{14}$ ;  
5  $X_1-X_2-X_3-X_4-X_5-X_6-X_7-X_8-X_9-X_{10}$ ;  
 $X_1-X_2-X_3-X_4-X_5-X_6-X_7-X_8-X_9-X_{10}-X_{11}$ ;  
 $X_1-X_2-X_3-X_4-X_5-X_6-X_7-X_8-X_9-X_{10}-X_{11}-X_{12}$ ;  
 $X_1-X_2-X_3-X_4-X_5-X_6-X_7-X_8-X_9-X_{10}-X_{11}-X_{12}-X_{13}$ ; and  
 $X_1-X_2-X_3-X_4-X_5-X_6-X_7-X_8-X_9-X_{10}-X_{11}-X_{12}-X_{13}-X_{14}$ ,

10

wherein  $X_2 - X_{10}$  are as defined;

$X_1$  is selected from the group consisting of Ile, Ala, Val, Leu, Ser, and Arg;

15

$X_{11}$  is selected from the group consisting of Ala, Ile, Val, Leu, Phe, Ser, Thr, Lys, His, and Glu;

$X_{12}$  is selected from the group consisting of Ala, Ile, Val, Leu, Phe, Gly, Ser, and Gln;

20

$X_{13}$  is selected from the group consisting of Arg, Lys, Thr, Val, Asn, Gln, and Gly; and

$X_{14}$  is selected from the group consisting of Ala, Ile, Val, Leu, Phe, Thr, Arg, Glu, and Gly.

25

3. The compound according to Claim 1 wherein said  $TMP_1$  and/or  $TMP_2$  are derivatized as set forth in one or more of the following:

30

one or more of the peptidyl [-C(O)NR-] linkages (bonds) have been replaced  
 by a non-peptidyl linkage such as a -CH<sub>2</sub>-carbamate linkage [-CH<sub>2</sub>-OC(O)NR-]; a  
 phosphonate linkage; a -CH<sub>2</sub>-sulfonamide [-CH<sub>2</sub>-S(O)<sub>2</sub>NR-] linkage; a urea [-  
 NHC(O)NH-] linkage; a -CH<sub>2</sub>-secondary amine linkage; or an alkylated peptidyl  
 linkage [-C(O)NR<sup>6</sup>- where R<sup>6</sup> is lower alkyl];

the N-terminus is a  $-NRR^1$  group; to a  $-NRC(O)R$  group; to a  $-NRC(O)OR$  group; to a  $-NRS(O)_2R$  group; to a  $-NHC(O)NHR$  group where  $R$  and  $R^1$  are hydrogen and lower alkyl with the proviso that  $R$  and  $R^1$  are not both hydrogen; to a succinimide group; to a benzyloxycarbonyl-NH- (CBZ-NH-) group; or to a  
5 benzyloxycarbonyl-NH- group having from 1 to 3 substituents on the phenyl ring selected from the group consisting of lower alkyl, lower alkoxy, chloro, and bromo;

the C terminus is  $-C(O)R^2$  where  $R^2$  is selected from the group consisting of lower alkoxy and  $-NR^3R^4$  where  $R^3$  and  $R^4$  are independently selected from the  
10 group consisting of hydrogen and lower alkyl.

4. The compound according to Claim 1 wherein all of the amino acids have a D configuration.

15 5. The compound according to Claim 1 wherein at least one of the amino acids has a D configuration.

6. The compound according to Claim 1 which is cyclic.

20 7. The compound according to Claim 1 wherein  $TMP_1$  and  $TMP_2$  are each

Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala. (SEQ ID NO: 1)

25 8. The compound according to Claim 1 wherein  $L_1$  comprises a peptide.

9. The compound according to Claim 8 wherein  $L_1$  comprises  $Y_n$ , wherein  $Y$  is a naturally-occurring amino acid or a stereoisomer thereof and  $n$  is 1 through 20.

30 10. The compound according to Claim 8 wherein  $L_1$  comprises  $(Gly)_n$ , wherein  $n$  is 1 through 20, and when  $n$  is greater than 1, up to half of the Gly residues may be substituted by another amino acid selected from the remaining 19 natural amino acids or a stereoisomer thereof.

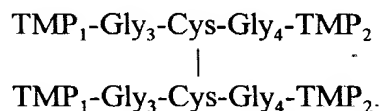
11. The compound according to Claim 8 wherein L<sub>1</sub> is selected from the group consisting of

(Gly)<sub>3</sub>Lys(Gly)<sub>4</sub> (SEQ ID NO: 6);  
(Gly)<sub>3</sub>AsnGlySer(Gly)<sub>2</sub> (SEQ ID NO: 7);  
(Gly)<sub>3</sub>Cys(Gly)<sub>4</sub> (SEQ ID NO: 8); and  
GlyProAsnGly (SEQ ID NO: 9).

12. The compound according to Claim 8 wherein L<sub>1</sub> comprises a Cys residue.

13. A dimer of the compound according to Claim 12.

14. The dimer according to claim 13 which is



15. The compound according to Claim 1 wherein L<sub>1</sub> comprises (CH<sub>2</sub>)<sub>n</sub>, wherein n is 1 through 20.

16. The compound according to Claim 1, which is selected from the group consisting of

IEGPTLRQWLAARA-GPNG-IEGPTLRQWLAARA (SEQ. ID NO: 9)

IEGPTLRQCLAARA-GGGGGGGG-IEGPTLRQCLAARA (cyclic) (SEQ. ID NO: 10)

IEGPTLRQCLAARA-GGGGGGGG-IEGPTLRQCLAARA (linear) (SEQ. ID NO: 11)

IEGPTLRQALAARA-GGGGGGGG-IEGPTLRQALAARA (SEQ. ID NO: 12)

IEGPTLRQWLAARA-GGGKGGGG-IEGPTLRQWLAARA (SEQ. ID NO: 13)

IEGPTLRQWLAARA-GGGK(BrAc)GGGG-IEGPTLRQWLAARA  
(SEQ. ID NO: 14)

IEGPTLRQWLAARA-GGGCGGGG-IEGPTLRQWLAARA (SEQ. ID NO: 15)

IEGPTLRQWLAARA-GGGK(PEG)GGGG-IEGPTLRQWLAARA  
(SEQ. ID NO: 16)

IEGPTLRQWLAARA-GGGC(PEG)GGGG-IEGPTLRQWLAARA  
(SEQ. ID NO: 17)

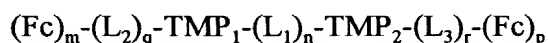
IEGPTLRQWLAARA-GGGNGSGG-IEGPTLRQWLAARA (SEQ. ID NO: 18)

IEGPTLRQWLAARA-GGGCGGGG-IEGPTLRQWLAARA

IEGPTLRQWLAARA-GGGCGGGG-IEGPTLRQWLAARA (SEQ. ID NO: 19);

IEGPTLRQWLAARA-GGGGGGGG-IEGPTLRQWLAARA (SEQ. ID NO: 20).

17. The compound according to Claim 1 or 2, which has the formula



wherein  $\text{L}_1$ ,  $\text{L}_2$  and  $\text{L}_3$  are linker groups which are each independently selected from the linker groups consisting of

$\text{Y}_n$ , wherein Y is a naturally-occurring amino acid or a stereoisomer thereof and n is 1 through 20;

$(\text{Gly})_n$ , wherein n is 1 through 20, and when n is greater than 1, up to half of the Gly residues may be substituted by another amino acid selected from the remaining 19 natural amino acids or a stereoisomer thereof;

[illegible][illegible][illegible][illegible][illegible][illegible][illegible][illegible][illegible][illegible][illegible]

GlyProAsnGly (SEQ ID NO: 9).

21. The compound according to Claim 18 wherein  $L_1$ ,  $L_2$ , or  $L_3$  comprises a Cys residue.

5

22. A dimer of the compound according to Claim 21.

23. The compound according to Claim 17 wherein  $L_1$ ,  $L_2$  or  $L_3$  comprises  $(CH_2)_n$ , wherein n is 1 through 20.

10

24. The compound according to Claim 1, which is selected from the group consisting of

*Sub 174*  
Fc-IEGPTLRQWLAARA-GPNG-IEGPTLRQWLAARA (SEQ. ID NO: 21)

15

Fc-IEGPTLRQWLAARA-GPNG-IEGPTLRQWLAARA-Fc (SEQ. ID NO: 22)

IEGPTLRQWLAARA-GGGGGGGG-IEGPTLRQWLAARA-Fc  
(SEQ. ID NO: 23)

20

Fc-GG-IEGPTLRQWLAARA-GPNG-IEGPTLRQWLAARA (SEQ. ID NO: 24)

Fc-IEGPTLRQWLAARA-GGGGGGGG-IEGPTLRQWLAARA  
(SEQ. ID NO: 25)

25

Fc-IEGPTLRQCLAARA-GGGGGGGG-IEGPTLRQCLAARA (cyclic)  
(SEQ. ID NO: 26)

Fc-IEGPTLRQCLAARA-GGGGGGGG-IEGPTLRQCLAARA (linear)  
(SEQ. ID NO: 27)

30

Fc-IEGPTLRQALAARA-GGGGGGGG-IEGPTLRQALAARA (SEQ. ID NO: 28)

Fc-IEGPTLRQWLAARA-GGKGGGG-IEGPTLRQWLAARA (SEQ. ID NO: 29)

35

Fc-IEGPTLRQWLAARA-GGGCGGGG-IEGPTLRQWLAARA (SEQ. ID NO: 30)

Fc-IEGPTLRQWLAARA-GGGNGSGG-IEGPTLRQWLAARA (SEQ. ID NO: 31)

5 Fc-IEGPTLRQWLAARA-GGGCGGGG-IEGPTLRQWLAARA

Fc-IEGPTLRQWLAARA-GGGCGGGG-IEGPTLRQWLAARA (SEQ. ID NO: 32)

10 Fc-GGGGG-IEGPTLRQWLAARA-GGGGGGGG-IEGPTLRQWLAARA  
(SEQ. ID NO: 33).

25. A method of increasing megakaryocytes or platelets in a patient in need thereof, which comprises administering to said patient an effective amount of a compound according to Claim 1.

15

26. The method according to Claim 25, wherein said amount is from 1 µg/kg to 100 mg/kg.

20

27. A pharmaceutical composition comprising a compound according to Claim 1 in admixture with a pharmaceutically acceptable carrier thereof.

28. A polynucleotide that encodes a compound according to claim 8.

29. A polynucleotide that encodes a compound according to claim 13.

25

30. A polynucleotide that encodes a compound according to claim 18.

31. A polynucleotide that encodes a compound according to claim 22.

30

32. A vector that comprises a polynucleotide according to any of claims 28-31.

33. A host cell that comprises a vector according to claim 32.



34. A method of producing a compound according to claims 8, 13, 18 or 22, which comprises growing a host cell according to claim 33 in a suitable nutrient medium and isolating said compound from said cell or nutrient medium.